UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 2724-452 / Zoecon Apex 5E

FROM: Ian Blackwell Ian Blackwell 3/12/92
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C) E 3/17/92

TO: Phillip Hutton PM 18
Insecticide-Rodenticide Branch
Registration Division (H7505C)

APPLICANT: Zoecon Corporation
12200 Denton Drive
Dallas, Texas 75234

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Methoprene [isopropyl (2E,4E,7S) -11-methoxy-3,7,11-trimethyl 2,4 dodecadienoate]	65.7
Inert Ingredients:.....	
Total	100.0%

BACKGROUND: The registrant, the Zoecon Corporation, has submitted acute oral toxicity, acute dermal toxicity, primary eye irritation, primary dermal irritation and dermal sensitization studies in support of the product Zoecon Apex 5E. The studies were conducted by SRI International. The MRID numbers are 421094-04 through -08.

RECOMMENDATION: RSB/PRS findings are:

1. All studies submitted are classified supplementary due to the test material being identified as "Zoecon Sample No. R174 SAN 800 I 66 EC" and not Zoecon Apex 5E. The registrant should submit a statement explaining the relationship between the test material and the registration product.

2. The primary eye irritation study is also classified as supplementary because:

   a. No scores were given for irritation of the test animals with unwashed eyes at 1 hour.
   b. No scores for discharge were given.

3. The dermal irritation study must be reconducted. The dermal irritation study is classified as supplementary, in addition to the above, because the test material was applied to an area of approximately 4 in^2. The guidelines call for the test area to be 1 in^2.

4. An acute inhalation toxicity study must be submitted.

LABELING:

1. Labeling will be assigned upon submission of the outstanding information.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (18). Report No.: LSC 2673-M027-91
Reviewer: Ian Blackwell Report Date: 10/25/91
MRID No.: 421094-04

Testing Facility: SRI International
Author(s): J.E. Schindler and R.C. Baldwin

Species: Sprague-Dawley rats
Sex: 5 males + 5 females
Age: males: 7-8 weeks; females: 9-10 weeks
Weight: males: 193-202g; females: 185-202g
Source: Simonsen Laboratories

Test Material: Zoecon sample #R174 SAN 800 I 66EC

Observation Days (Post Exposure): (14); other ( )

Quality Assurance (40 CFR §160.12): Included

Conclusion:

1. LD50 (mg/kg): Males (M) = > 5.1 g/kg
   Females (F) = > 5.1 g/kg
   Combined(C) = > 5.1 g/kg

2. Toxicity Category:
   Classification: core-supplementary

Procedure (Deviations From §81-1):
Test material not identified as the product for registration.

Results:

Reported Mortality

Dosage (g/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
5.1 g/kg	0/5	1/5	1/10

Observations: Signs of toxicity were: (in all females) ataxia, lack of activity, diarrhea, hypothermia and weakness. All males appeared normal throughout the study.

Gross necropsy observations were: diarrhea in one female and a firm, yellow fatty, mass in the groin in another female. No abnormalities were observed in males upon gross necropsy.

4

DATA REVIEW FOR
ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager (PM): 18

Reviewer: Ian Blackwell
MRID No.: 421094-07

Report No.: LSC 2673-M028-91
Report Date: 10/25/91

Testing Laboratory: SRI International
Author(s): J.E. Schindler and R.C. Baldwin

Species : New Zealand White rabbits
Age : 14 to 15 weeks
Sex : 5 males + 5 females
Wt.: males: 2.88-2.94 kg; females: 2.76-3.13 kg
Source: Western Oregon Rabbit Company

Test Material: Zoecon sample No. R174 SAN 800 I 66EC
Dosage: 2.1 g/kg

Quality Assurance (40 CFR §160.12): Included

Summary:

LD50: _____
Toxicity Category: _____
Classification: core - supplementary

Procedure (Deviations From §81-2):
The test material was not identified as the product for registration.

Results:

1. Reported Mortality

Dosage (g/kg)	Mortality Ratio (number killed/number tested)		
	Males (M)	Females (F)	Combined (C)
2.1 g/kg	0/5	0/5	0/10

2. Observations: No systemic signs of toxicity were observed. All rabbits displayed slight-to-moderate erythema and edema. Desquamation and fissuring were also observed.

DATA REVIEW FOR
PRIMARY EYE IRRITATION TESTING (§81-4)

Product Manager (PM): 18
Reviewer: Ian Blackwell
MRID No: 421094-06

Report No.: LSC 2673-M030-91
Report Date: 10/25/91

Testing Laboratory: SRI International
Author(s): J.E. Schindler and R.C. Baldwin

Species: New Zealand White rabbit Sex: 3 males + 3 females
Source: Western Oregon Rabbit Company
Age: 14 to 15 weeks

Test Material : Zoecon Sample No. R174 SAN 800 I 66EC
Dosage: 0.1 ml

Quality Assurance (40 CFR §160.12): Included

Summary:

Toxicity Category:
Classification: core - supplementary

Procedure (Deviation From §81-4):
Test material not identified as the product for registration.
Irritation scores at 1 hour not given for test animals whose eyes were unwashed.
No scores for discharge were given.

Results:

	Observations (number "positive"/number tested.							
	Hour 1	Days 1	2	3	4	7	14	21
Cornea	---	0/6	0/6	0/6	---	---	---	---
Iris	---	0/6	0/6	0/6	---	---	---	---
Conjunctivae								
Redness	---	6/6	3/6	0/6	---	---	---	---
Chemosis	---	0/6	0/6	0/6	---	---	---	---
Discharge	---	---	---	---	---	---	---	---

Comments: Three additional rabbits were dosed and had their eyes washed for thirty seconds approximately 30 seconds after administration of the test material. No corneal irritation was displayed and 1/3 displayed grade 1 irritation of the iris. All displayed conjunctival irritation at 1 hour of grades 3 and 2. No redness was displayed after 48 hours in any test animals. No chemosis or discharge was displayed after 1 hour.

DATA REVIEW FOR
DERMAL IRRITATION TESTING (§81-5)

Product Manager (PM): 18

Reviewer: Ian Blackwell
MRID No.: 421094-05

Report No.: LSC 2673-M029-91
Report Date: 10/25/91

Testing Laboratory: SRI International
Author(s): J.E. Schindler and R.C. Baldwin

Species: New Zealand White rabbits
Age : 14 to 15 weeks
Weight: 2.89 to 3.15 g
Source : Western Oregon Rabbit Company

Test Material : R174 SAN 800 I 66EC
Dosage : 0.5 ml to 4 in^2 area

Quality Assurance (40 CFR §160.12): Included

Summary: Toxicity Category: _____

Classification: core - supplementary

Procedure (Deviations From §81-5):
The test material was not identified as the product for registration.
The test material was applied to an area of approximately 4 in^2, not 1 in^2 as per guidelines.

Results: At approximately one hour after patch removal each animal displayed very slight erythema. Twenty four hours after treatment, 4/6 displayed well-defined erythema and 2/6 displayed very slight erythema. At 48 hours 5/6 displayed very slight erythema and 6/6 displayed very slight erythema at 72 hours. On Day 7, 1/6 displayed moderate-to-severe erythema, 2/6 displayed well-defined erythema and 3/6 displayed very slight erythema. On Day 14, 2/6 displayed very slight erythema. On Day 21, 1/6 displayed well-defined erythema and 1/6 displayed very slight erythema. The only edema displayed was by 1/6 on Day 21.

DATA REVIEW FOR
DERMAL SENSITIZATION TESTING (§81-6)

Product Manager:(PM) 18

Reviewer: Ian Blackwell
MRID No.: 421094-08

Report No.: LSC 2673-M031-91
Report Date: 10/25/91

Testing Laboratory: SRI International
Author(s): J.E. Schindler and R.C. Baldwin

Species: Hartley albino guinea pigs
Sex : 21 males + 21 females Age: 4 weeks
Weight: 252 to 335 g
Source: Simonsen Laboratories

Test Material : R174 SAN 800 I 66EC, Lot ED 016
Dosage : 100% induction, 50% challenge
Positive Control: Dichloronitrobenzene

Quality Assurance (40 CFR §160.12): Included

Method: Buehler Method

Summary:

This product is/is not a dermal sensitizer.

Classification: core - supplementary

Procedure (Deviation From §81-6):
Test material not specified as product for registration.

Results: Throughout the three induction treatments, animals treated with the test material displayed faint to very faint erythema with one male and three females displaying no erythema. Twenty-four hours after challenge, 3/10 animals displayed moderate, 3/10 displayed faint, and 4/10 animals displayed very faint erythema. Forty-eight hours after challenge, 2/10 animals displayed moderate, 6/10 displayed faint, and 2/10 displayed very faint erythema. Twenty-four hours after rechallenge, 3/10 displayed very faint, 4/10 displayed faint and 3/10 displayed moderate erythema.

Twenty-four hours after treatment of the naive control animals, 1/10 displayed faint and 5/10 displayed very faint erythema.

During induction of the positive control animals, faint to very faint erythema and one score of moderate erythema were displayed. Twenty-four hours after challenge, 1/6 displayed strong, 3/6 displayed moderate, 1/6 displayed faint and 1/6 displayed very faint erythema.

Tox Chem No. 028AAA File Last Updated _____ Current Date 1/28/92

Study/Animal/Lab/Date	Material	EPA Accession Number	Results: LD50, LC50, etc.	Tox. Cat.	CORE Grade
Acute oral toxicity/ LSC 2673-M027-91/ rat/ SRI International/ 10-25-91	Methoprene [isopropyl (2E,4E,7S)-11-methoxy -3,7,11-trimethyl 2,4 dodecadienoate 65.7%	421094-04			supple-mentary
Acute dermal toxicity/ LSC 2673-M028-91/ rabbit/ SRI Inter-national/ 10-25-91		421094-07			supple-mentary
Primary eye irritation LSC 2673-M030-91/ rabbit/ SRI Inter national/ 10-25-91		421094-06			supple-mentary
Primary dermal irrit./ LSC 2673-M029-91/ rabbit / SRI Inter-national/ 10-25-91		421094-05			supple-mentary
Dermal sensitization/ LSC 2673-M031-91/ guinea pig/ SRI International/10-25-91		421094-08			supple-mentary